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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/286,166	04/05/1999	DANA M. FOWLKES	CPI-012CP4BC	4623

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EXAMINER
BRANNOCK, MICHAEL T

ART UNIT	PAPER NUMBER
1646	18

DATE MAILED: 12/14/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/286,166	Fowlkes, DM et al.
Examiner	**Art Unit**
Michael Brannock, Ph.D.	1646

-- Th MAILING DATE of this communication appears on th cover sh et with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Oct 5, 2001

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 43-58 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 43-58 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Status of Application: Claims and Amendments

1. Applicant's amendments of Paper 11 (3/1/01), Paper 13 (6/25/01) and Paper 16 (10/5/01), have been entered in full.

2. Claims 43-58 are pending

Specification

3. The instant specification appears to be incompliance with the rules regarding sequence disclosures.

Maintained Rejections:

Double Patenting

4. Claims 43-51 stand and new claims 52-58 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-47 of U.S. Patent No. 6100042, as set forth in item 6 of Paper 9. It is acknowledged that Applicant intends to address the propriety of the this rejection upon an indication that the application is otherwise in condition for allowance.

5. Claims 43, 44, 45, 47, 50 and 51 stand rejected and new claims 52, 54, 55, 57 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5284746 in view of

Kang, YS. et al. Mol. Cell. Biol. 10(2582-2590)1990, as set forth in item 8 of Paper 9 and reiterated below:

U.S. Patent No. 5284746 discloses a transformed yeast cell comprising a reporter gene (see col 12, L43, e.g. LacZ see col 12, L65-66) under the control of a pheromone-responsive promoter (see col 12, L42; e.g. FUS1 promoter see col 12, L48-56), a heterologous mammalian G-protein coupled receptor gene (β2- adrenergic receptor, for example, see col 1), wherein said receptor is a hybrid receptor comprising intracellular sequences from yeast and sequences from heterologous receptors (see col 3, L2), wherein said yeast receptor sequences are STE2 sequences (see col 4, L33), wherein said receptor is capable of inducing yeast pheromone response (see col 4, L5), each gene being under the control of a separate promoter (second construct) (see col 12, L 41), and a mutation in the ste2 gene causing increased sensitivity to receptor activation (see col 10, L8-9).

The disclosure of U.S. Patent No. 5284746 does not teach a hybrid Gα protein comprising yeast Gα nor an otherwise heterologous Gα protein. Kang, Y.S. et al. (supra) disclose heterologous yeast/mammalian hybrid Gα proteins expressed in yeast that complement the cell cycle arrest in cells lacking endogenous Gα (scg1 mutant cells) (see page 258, 3rd para). Conversely, U.S. Patent No. 5284746 teaches that heterologous hybrid yeast\ mammalian G-protein-coupled-receptors can induce cell cycle arrest in cells lacking the endogenous receptor (see col 4, line 25-35). Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made, with reasonable expectation of success, to use hybrid Gα proteins

instead of hybrid G-protein receptors in the assay disclosed in U.S. Patent No. 5284746. The motivation to do so was provided by Kang et al. who stated that portions of mammalian Gα proteins (Gαi) which bind to mammalian receptors but do not interact with yeast βγ subunits could be made to do so by expressing them as hybrid proteins containing yeast sequences (See table 2).

Applicant argues that the Kang et al. hybrids do not work and therefore one of skill in the art would not be motivated to use the teachings of Kang et al. In support of this assertion Applicant argues that the "Kang et al. hybrids are unable to elicit signal transduction and consequent mating because they are unable to interact with the receptor (pheromone)". Further, Applicant argues that the hybrids of the instant invention are in contrast to those of Kang because the hybrids of the instant invention "not only interact with the yeast Gβγ subunit, but also interact with the receptor (i.e., the heterologous G-protein-coupled receptor) thereby permitting signal transduction". Furthermore, applicant argues that the failure of the Kang et al. hybrids to produce a detectable phenotype certainly cannot be said to provide an expectation of success. These arguments have been fully considered but not deemed persuasive because they rely on: (a) a mischaracterization of the experiments of Kang et al., (b) a false comparison between the hybrids of Kang et al. and the instant hybrids, and (c) a misunderstanding of the meaning of the word "phenotype" and/or a misreading of the Kang paper.

Regarding (a): the hybrids of Kang et al. do work. Kang report that the Gα subunit hybrids are able to overcome the *scg1* growth arrest phenotype by interacting with the yeast Gβγ

subunit, but they do not interact with the yeast pheromone receptors (see the Abstract). One of ordinary skill in art appreciates that Kang is demonstrating an intriguing property of yeast cells that had been suggested by other genetic experiments. It is the yeast Gβγ subunit and not the Gα subunit that is responsible for signal transduction; this is in contrast to most animal systems wherein the Gα subunit couples to downstream effectors (see the DISCUSSION, especially the 2nd paragraph). One of ordinary skill in the art would not have interpreted this demonstration to suggest that the Kang hybrids do not work. To the contrary, the hybrid receptors bind yeast Gβγ subunit and reverse the *scg1* growth arrest phenotype.

Regarding (b): Applicant draws a false comparison between the Kang hybrids and the instant hybrids. Applicant asserts that the Kang hybrids do not interact with receptors (endogenous yeast pheromone receptor) but that the instant hybrids do interact with receptors (heterologous mammalian receptors). This is an "apples and oranges" comparison because Kang was not testing for an interaction between the hybrids and heterologous mammalian receptors; only yeast pheromone receptors where present in the Kang experiments.

Regarding (c): the hybrids of Kang do produce a detectable phenotype. The hybrids of Kang complement the growth arrest phenotype of *scg1*; one of ordinary skill in the art appreciates that this activity is a phenotype, and that it was successfully measured by Kang (see Table II). Thus there is no basis for Applicant's assertion "that the failure of the Kang et al. hybrids to produce a detectable phenotype certainly cannot be said to provide an expectation of success". To the contrary Kang demonstrate and that mammalian/yeast G-alpha hybrids can be

made to function in yeast. They conclude, "These results indicate sufficient conservation of structure between the yeast and mammalian Gα proteins to allow the function of appropriate domains in the hybrids and suggest that, like intact Gαs and Gαi, these proteins can interact with Gβ but not with the pheromone receptors" see page 2588, col 2, middle of first full paragraph, emphasis added.

6. Claims 46, 47, 48, 49 stand rejected and new claims 53 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5284746 and Kang, YS. et al. Mol. Cell. Biol. 10(2582-2590)1990 for the reasons put forth above regarding claims 43, 44, 45, 47, 50, 51, 52, 54, 55, 57 and 58 and in further view of Chang et al.. (Cell 63:999-1011,1990), as set forth in item 9 of Paper 9 and reiterated below.

The disclosure of U.S. Patent No. 5284746 in view of Kang, YS. et al. includes the elements of claims 43, 44, 45, 47, 50, 51, 52, 54, 55, 57 and 58 as discussed above, with the exception that neither reference teach a mutation in the FAR1 gene which permits transcriptional activation of pheromone-responsive genes without cell cycle arrest. Chang et al. teach that mutations in the FAR1 gene permit transcriptional activation of pheromone-responsive genes without cell cycle arrest (see the abstract and Figure 1). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made, with reasonable expectation of success, to include mutations in the FAR1 gene (as disclosed by Chang et al.) when using the assay disclosed in U.S. Patent No. 5284746, modified as taught by Kang et al. The motivation

to do so is provided by the teachings of Chang et al. who state that FAR1 mutations allow for the observation of pheromone-responsive transcription in dividing cells, i.e. in the absence of cell cycle arrest (see para 1, pg 1001 of Chang et al.) - pheromone-responsive transcription being required to drive reporter gene expression as taught U.S. Patent No. 5284746 (see col 12).

Applicant correctly points out that claim 48 was not included in the original rejection yet the claim recites the limitation of a mutation in the FAR1 gene; this was an obvious inadvertent clerical error.

Applicants arguments concerning the applicability of U.S. Patent No. 5284746 and Kang et al. against the instant claims have been addressed above. Applicant further argues that the Chang et al. reference does not make up any deficiencies in the U.S. Patent No. 5284746 and Kang et al. references and nor would one of ordinary skill in the art would not have been motivated to combine the Chang et al reference with U.S. Patent No. 5284746 and Kang et al. to arrive at the instant claimed invention. Applicant appears to base these arguments on the idea that the motivation to combine these references could come from a reading of Applicant's specification, however no specific arguments appear to be put forth to support Applicant's position.

The Sledziewski patent teaches that a heterologous reporter gene such as LacZ can be placed under the control of the BAR1 promoter (see cols 3 and 4). The BAR1 promoter responds to activation of the heterologous receptor by inducing transcription of the reporter LacZ gene. Thus, the transcription of the lacZ reporter is now under the control of the pheromone response

pathway. It is simply a matter of common sense, that it is preferable to have a signal that is amplified by the continued division of cells (not undergoing cell-cycle arrest), however, at the time of filing of the Sledziewski patent there appears to have been no good way to accomplish this in that system. The discovery by Chang et al. solves this problem. The most obviating teaching is that Chang et al. state that FAR1 mutations allow for the observation of pheromone responsive transcription in dividing cells (see para 1, pg 1001); the ability to observe pheromone responsive transcription being exactly what the lacZ reporter gene described in the Sledziewski patent is intended to accomplish.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Fridays from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

December 8, 2001

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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